DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/20/08 has been entered.

Claim Rejections – 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 107 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 107 recites, “The biosensor according to claim 74, wherein the mammalian subject is pretreated with platelet derived growth factor at the site of implantation”. The claim language is directed to method steps, but claim 74, upon which claim 107 depends, is an apparatus claim. It is unclear whether an apparatus or a method is being claimed. For the purpose of this examination only, the claim is being interpreted as being directed toward an apparatus, wherein the language regarding the method steps does not appear to further limit the apparatus, particularly

since the applicants' remarks filed 5/20/08 (see p. 9) establish that the growth factor is not part of the biosensor.

Claim Rejections – 35 USC §102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 74, 76-78, 80-83, and 107 are rejected under 35 U.S.C. 102(b) or in the alternative under 35 U.S.C. 103(a) as being anticipated by US Patent No. 5,368,028 to Palti. Palti teaches an implantable physiological or pathophysiological biosensor comprising cells (see entire document, especially col. 9, lines 16-31 of Palti) coupled to an electrical interface (see entire document, especially col. 6, lines 14-19; col. 11, ,lines 4-25 of Palti) and adapted to be electrically coupled to endogenous tissue or cells when implanted into a mammalian subject at a site distant from a natural site for a

physiological or pathophysiological function of the subject (see entire document, especially col. 6, line 66-col. 7, line 9; col. 11, line 44-col. 12, line 26 of Palti). The cells are adapted to electrically couple with endogenous tissue or cells via the transmission means, such as the transmitter that sends the processed signals through the skin, the implanted electrodes and amplifier for generating an electric field, or an induction coil or coupling capacitive signal transferor. The cells are capable of monitoring a blood borne chemical, physiological, or pathophysiological function of the subject (see entire document, especially col. 9, line 16-col. 10, line 34 of Palti) and are further capable of producing at least a hormone, wherein beta cells from the islets of Langerhans, for example, are capable of producing insulin, which is a hormone.

In the alternative, it would have been obvious to one of ordinary skill in the art to produce the cells of Palti by modifying stem cells, since the production of a differentiated cell by modifying a stem cell is a well-known process.

As to the language “in vitro or ex vivo modified stem cells”, the applicant should note that this is “product-by-process” language, wherein the structure implied by the process steps, rather than the process itself, is given patentable weight. See MPEPE 2113. In the case of “in vitro or ex vivo modified stem cells”, the structure implied by the process of modifying stem cells either in vivo or ex vivo is merely a developed or differentiated cell. For example, the modification of stem cells in vitro or ex vivo may result in beta cells. Claim 76 contains more language regarding the process by which the cells are produced, wherein the product-by-process language again implies no more than another cell, such as a beta cell, which may be produced by cellular engineering or

natural cell differentiation, wherein natural cell differentiation is a modification of a stem cell.

As to the language "when implanted into a mammalian subject at a site distant from a natural site for a physiological or pathophysiological function of the subject", the applicants should note that this is merely "intended use" language which cannot be relied upon to define over the prior art, since Palti teaches all of the claimed structural limitations and their recited relationships. Ex parte Masham 2 USPQ2d 1647 (BPAI 1987). The device of Palti is certainly capable of implantation at any site in a mammalian subject in which size permits, wherein the site may clearly be distant form a natural site for a physiological or pathophysiological function of the subject, and further is certainly capable of being electrically coupled to tissue at such a site.

Regarding claim 75, beta cells, for example, are capable of producing endothelial growth factor (VEGF).

Regarding claim 78, the physiological or pathophysiological variable is a level of activity of at least blood glucose (see entire document, especially col. 9, lines 25-55 of Palti).

Regarding claims 80-82, the biosensor clearly appears capable of being implanted in any mammal. The language "when implanted into a mammalian subject" is "intended use" language which cannot be relied upon to define over the prior art, since Palti teaches all of the claimed structural features and their recited relationships. Ex parte Masham 2 USPQ2d 1647 (BPAI 1987).

Regarding claim 83, the cells are incorporated within a device (see entire document, especially col. 10, line 41-col. 12, line 61 of Palti).

Regarding claim 107, the applicants should refer to the rejection under 35 U.S.C. 112, 2nd paragraph, set forth above.

Claims 74-76, 80-84, and 107 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent Application Publication No. 2003/0211088 to Field. Field teaches an implantable device comprising an in vitro or ex vivo modified stem cell coupled to an electrical interface 12 and adapted to be electrically coupled to endogenous tissue or cells when implanted into a mammalian subject at a site distant from a natural site for physiological or pathophysiological function of the subject (see entire document, especially fig. 1; paragraphs 13, 18, 23-25, 40-42, and 62 of Field). The cells (cardiomyocytes) can monitor a blood-borne chemical, physiological, or pathophysiological variable associated with the physiological and pathophysiological function of the subject, wherein the applicants' specification identifies cardiac cells/cardiomyocytes as capable of such monitoring (see p. 9, line 25-p.10, line 9; p. 11, line 4-6; p. 22, line 25-p. 23, line 15 of the instant specification, for example), and cardiomyocytes can produce at least a growth factor, such as vascular endothelial growth factor.

As to the language "when implanted into a mammalian subject at a site distant from a natural site for a physiological or pathophysiological function of the subject", the applicants should note that this is merely "intended use" language which cannot be

relied upon to define over the prior art, since Field teaches all of the claimed structural limitations and their recited relationships. Ex parte Masham 2 USPQ2d 1647 (BPAI 1987). The device of Field is certainly capable of implantation at any site in a mammalian subject in which size permits, wherein the site may clearly be distant from a natural site for physiological or pathophysiological function of the subject.

The examiner notes the use of the term "biosensor" in the preamble of claim 74. However, the term fails to denote any structural features not already present in the device of Field. Furthermore, Field teaches all of the structural features claimed in the body of claim 74 and their recited relationships as set forth above. If the device of Field lacks a structural feature necessary for its function as a "biosensor", then it would appear that the applicants have failed to include an essential element of the invention (i.e. a problem under 35 U.S.C. 112, 1st paragraph).

Regarding claim 75, cardiomyocytes are capable of producing vascular endothelial growth factor (VEGF).

Regarding claim 76, the cells are genetically engineered (see entire document, especially paragraphs 23-28 of Field).

Regarding claims 80-82, the device is capable of being implanted in any mammal.

Regarding claims 83 and 84, the cells are incorporated within a device such as an electronic pacemaker (see entire document, especially fig. 1; paragraphs 40, 41, and 62 of Field).

Regarding claim 107, the applicants should refer to the rejection under 35 U.S.C. 112, 2nd paragraph, set forth above.

Response to Arguments

Applicant's arguments filed 5/20/08 have been fully considered but they are not persuasive.

Regarding the Palti reference, the applicants submits that a stem cell is a physical entity and not a process step and that a modified stem cell is also a physical entity and not a process step. At no time has the examiner made any argument that either a stem cell or a modified stem cell is a process step. The examiner *has* already repeatedly explained that the language "modified stem cell" and "in vitro or ex vivo modified stem cells" *are* product-by-process language, and the applicants have also repeatedly been directed to MPEP 2113 for further explanation of such language and the treatment of such language. The applicants further request that the examiner consider the actual structure of the claimed subject matter "rather than some structure that might hypothetically evolve from Applicants' claimed subject matter". The examiner *has* considered the actual structure of the claimed subject matter as repeatedly explained in the previous Office action and above, wherein the actual structure of the claimed subject matter is no more than a developed or differentiated cell. As also stated in the previous Office action and explained in MPEP 2113, the burden is on the applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. The applicants have provided no such

evidence. Applicants' remarks as to Palti's disclosure or lack thereof as to a stem cell or modified stem cell is not evidence showing such a structural difference and is therefore irrelevant. Additionally, the applicants' alleged observation that Palti does not disclose cells producing a growth factor is inaccurate. Whether or not Palti explicitly discloses production of a growth factor, a beta cell *can* or is inherently capable of production of a growth factor (VEGF; see the rejection set forth above and in the previous Office action for details), wherein claim 74 recites that the cells "can produce . . . a growth factor". Further, the allegation that Palti fails to disclose that cells producing a coagulation factor, serotonin, or a receptor should be employed is irrelevant, since the capability of producing each item is claimed in the alternative, and the examiner has already established that the cells can produce a growth factor or a hormone.

As to the Field reference, the applicants' arguments as to "distant implantation" of the sensor appears to refer to the recitation "adapted to be electrically coupled to endogenous tissue or cells when implanted into a mammalian subject at a site distant from a natural site". The examiner has already addressed this recitation in the previous Office action (see the rejection and the "Response to Arguments" section) and in the rejection set forth above. With regard to Field failing "to disclose cells that monitor to blood-borne a blood-borne chemical, physiological, or pathophysiological variable associated with the physiological or pathophysiological function of the subject" [sic], as explained in the previous Office action and above, Field discloses cells that monitor a physiological or pathophysiological variable associated with the physiological or

pathophysiological function of the subject. The language of claim 1 fails to clearly set forth that the monitored physiological or pathophysiological variable be "blood-borne".

Regarding the applicants' comment that Field fails to disclose administration of the biosensor to a mammalian subject pretreated with platelet derived growth factor at the site of implantation, the applicants should note that claim 107 is an apparatus claim and not a method claim. The limitation as to pretreatment of the site of implantation fails to further limit any aspect of the claimed apparatus, and therefore, bears no patentable weight.

Therefore, the rejections of claims as being anticipated by Palti or Field stand.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PATRICIA C. MALLARI whose telephone number is (571)272-4729. The examiner can normally be reached on Monday-Friday 10:00 am-6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Charles Marmor, II can be reached on (571) 272-4730. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Patricia C. Mallari/
Examiner, Art Unit 3735